ABSTRACT

Objective: This study aimed to determine the prevalence of nasopharyngeal tuberculosis among patients who were initially assessed to have a nasopharyngeal mass and subsequently underwent biopsy in a Philippine Tertiary General Hospital from Year 2013 to 2015.

Methods:

Design: Case Series
Setting: Tertiary National University Hospital
Participants: All patients with nasopharyngeal mass identified from January 2013 to December 2015 from a hospital wide census who underwent biopsy were investigated using chart and histopathology review. The prevalence of tuberculosis, malignancies and other findings were determined.

Results: Among 285 nasopharyngeal biopsies done between 2013 and 2015, 33 (11.6%) were histologically compatible with nasopharyngeal tuberculosis, 177 (62.1%) were different types of nasopharyngeal carcinoma, 59 (20.7%) were chronic inflammation, 4 (1.4%) were lymphoma, 5 (1.8%) were normal, and 7 (2.5 %) had diagnoses other than those above.

Conclusion: This study suggests a relatively high prevalence rate (11.6%) of nasopharyngeal tuberculosis in patients who have a nasopharyngeal mass. This indicates that nasopharyngeal tuberculosis should always be a differential when confronted with a mass in the nasopharynx especially in tuberculosis endemic areas.

Keywords: nasopharyngeal tuberculosis; prevalence; censuses; tertiary care centers; Philippines; carcinoma; nasopharynx; biopsy; tuberculosis; lymphoma

While the majority of tuberculosis infection is found in the lungs, tuberculosis can manifest in the head and neck region including cervical lymph nodes, parotid, the larynx, middle ear and tonsils. Nasopharyngeal tuberculosis (NPTB) is rarer and to the best of our knowledge, has been characterized in only a few case reports and series worldwide. There has only been one published case report in the Philippines.
Based on available literature, NPTB usually presents with nasopharyngeal mass associated with cervical lymphadenopathy as well as nasal, ocular and otologic symptoms.\textsuperscript{6,10} These findings overlap with the clinical presentation of nasopharyngeal malignancies, posing important diagnostic and therapeutic issues.\textsuperscript{6,11-15}

The study aimed to determine the prevalence of nasopharyngeal tuberculosis among patients who underwent nasopharyngeal biopsy in the Philippine National University Hospital from January 2013 to December 2015.

METHODS

With Institutional Ethical and Technical Review Board approval (UPMREB ORL - 2016-387-01), this descriptive case series sought to review records of patients of any age who were previously assessed to have a nasopharyngeal mass on endoscopy and who eventually underwent nasopharyngeal mass biopsy at the Philippine General Hospital from January 1, 2013 to December 31, 2015.

Patients who underwent nasopharyngeal mass biopsies were initially identified from the Department of Otorhinolaryngology census and logbooks of the in-patient and out-patient operating rooms.

Records were retrieved by the first author and basic demographic (age and sex) and histopathologic data were collated and recorded using Microsoft Office Professional Plus 2010 for Windows (Microsoft Corporation, Redmond, WA USA).

Excluded were patients whose biopsies were deferred due to other health reasons, who underwent intranasal (instead of nasopharyngeal) mass biopsies and those with incomplete entries. Patients who had previous recurrences of the condition and appeared twice in the registry were considered as one patient.

The final histopathological diagnoses were retrieved from the database of histopathology results at the Department of Laboratories. Full hospital chart reviews were attempted on all patients with NPTB.

Descriptive statistics were used to define demographics and summarize and describe the data. The prevalences of each of the diagnoses were computed based on the data. The different prevalences were then described.

RESULTS

Among the 285 nasopharyngeal biopsies we identified between 2013 and 2015, 33 (11.6%) were histologically compatible with nasopharyngeal tuberculosis (NPTB), 177 (62.1%) were different types of nasopharyngeal carcinoma (NPCA), 59 (20.7%) were interpreted as chronic inflammation, four (1.4%) were lymphoma, five (1.8%) were normal, and seven (2.5%) were diagnosis other than those mentioned.

The mean age of all patients with nasopharyngeal mass was 43.47 years old. The mean age of patients with nasopharyngeal carcinoma was 47.84 years old while the mean age of patients with nasopharyngeal tuberculosis was younger at 29.15 years old. The mean age of patients with chronic inflammation and lymphoma were 38.82 and 40.5 years old, respectively. The youngest patients with NPCA, chronic inflammation, NPTB and lymphoma were 15, 15, 14 and 17 years old, respectively. The oldest patients with NPCA, chronic inflammation, NPTB and lymphoma were 78, 70, 60 and 66 years old, respectively.

The patients had variable distributions among different age groups. The distribution of disease according to age group is shown in Table 1. In terms of sex, the ratio of nasopharyngeal carcinoma and chronic inflammation were almost the same at 3:1. On the other hand, the sex ratio for nasopharyngeal tuberculosis and lymphoma were the same and equal at 1:1. The distribution of patients is shown in Table 2.

Of the 33 patients with NPTB, only seven complete patient charts were retrieved. Most of the records of other patients had been transferred to their local Tuberculosis Treatment Center or were missing. Among the seven patients whose complete charts were reviewed, two had a previous history of pulmonary tuberculosis and had been treated with anti-tuberculosis chemotherapy and one had a history of unrecalled chronic lung illness which could also be pulmonary tuberculosis. All the seven patients had presence of cervical lymphadenopathy which prompted the initial medical consult. There was no mention of history of Human Immunodeficiency Virus infection, multidrug resistant tuberculosis infection or diabetes mellitus in the charts of the seven NPTB patients.

### Table 1. Distribution of Disease according to Age Group

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Nasopharyngeal Carcinoma (%)</th>
<th>Nasopharyngeal Tuberculosis (%)</th>
<th>Chronic Inflammation (%)</th>
<th>Lymphoma (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-20</td>
<td>5 (2.8%)</td>
<td>10 (30.3%)</td>
<td>9 (15.3%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>21-55</td>
<td>127 (71.8%)</td>
<td>20 (60.6%)</td>
<td>38 (64.4%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>56-70+</td>
<td>45 (25.4%)</td>
<td>3 (9%)</td>
<td>12 (20.3%)</td>
<td>1 (25%)</td>
</tr>
</tbody>
</table>

### Table 2. Distribution of Disease according to Sex

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPCA (N=177)</td>
<td>132 (74.6%)</td>
<td>45 (25.4%)</td>
</tr>
<tr>
<td>NPTB (N=33)</td>
<td>17 (51.5%)</td>
<td>16 (48.5)</td>
</tr>
<tr>
<td>Chronic Inflammation (N=59)</td>
<td>45 (76.3%)</td>
<td>14 (23.7%)</td>
</tr>
<tr>
<td>Lymphoma N=4</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
</tr>
</tbody>
</table>
DISCUSSION

Nasopharyngeal Tuberculosis (NPTB) has been described prior to the advent of the anti-tuberculosis antibiotics in 1936 by Graff who identified a high presence (82%) of nasopharyngeal tuberculosis by histology in 118 pulmonary tuberculosis cases. After the emergence of anti-tuberculosis medications, there was a dramatic decrease in cases of nasopharyngeal tuberculosis. A 1976 survey of 843 cases of pulmonary tuberculosis by Rohwedder found 16 patients with tuberculosis of the upper respiratory tract and only one of these had nasopharyngeal tuberculosis. The recent worldwide upsurge in the incidence of nasopharyngeal tuberculosis in the literature could be due to increased awareness of disease, improvement of knowledge regarding the entity, improved diagnostic techniques and of course, increase in incidence of the disease itself.

Most of the literature on the topic is only in the form of case reports and series that were gathered over many years and are not enough to give a clear picture of the prevalence of the illness. As of this writing, we could find no other studies detailing its prevalence. Based on our study, the prevalence of NPTB can reach as high as 1.1 for every 10 nasopharyngeal biopsies. This prevalence of nasopharyngeal tuberculosis is second only to nasopharyngeal carcinoma and even higher than lymphoma.

There are several important implications of the results of our study. First, clinicians usually have two main differential diagnoses when faced with a nasopharyngeal mass—nasopharyngeal carcinoma or lymphoma. The results of our study would add nasopharyngeal tuberculosis to the differentials especially in areas where tuberculosis is endemic. These three diagnoses each entail totally different managements and accurate diagnosis is necessary to provide proper treatment. The additional differential should guide other medical specialists. Pathologists must thoroughly analyse histopathologic slides especially those with chronic inflammatory patterns because hidden in the sea of inflammatory cells might be islands of tuberculosis or granulomatous lesions that may be overlooked. Pathologists should also be careful in making diagnosis because concomitant TB infection of the nasopharynges of patients with nasopharyngeal carcinoma may be present. Radiologists should consider the possibility of nasopharyngeal tuberculosis in interpreting CT Scans of patients with a nasopharyngeal mass. The possibility of nasopharyngeal tuberculosis should also be mentioned in patient education, and patient anxiety may be decreased by the knowledge that not all nasopharyngeal masses are cancer.

There are also important implications related to the safety of clinicians. Although it is the usual practice for otorhinolaryngologists to wear standard personal protective equipment in performing nasopharyngeal biopsies, the high prevalence of tuberculosis in patients with nasopharyngeal mass will require additional precautions such as wearing N95 masks instead of regular masks and ultraviolet disinfection after surgery. As patients with nasopharyngeal tuberculosis may have other co-morbidities such as HIV infection, these additional precautionary measures mentioned are well-justified.

Diagnosis of NPTB in previous reports were done initially by nasal endoscopy, biopsy and culture of tuberculous bacilli from secretions and nasopharyngeal tissue. Histopathology of the biopsied nasopharyngeal may also be helpful since results of TB culture may cause delays in diagnosis up to 6 weeks. Additional radiologic examinations may also be helpful such as CT scan and MRI. A study in China reported that a presence of necrosis and striped pattern in nasopharyngeal lesions and lack of invasion of regional structures as seen in CT and MRI of 36 NPTB patients may suggest the diagnosis of NPTB instead of malignancy.

In terms of management, previous reports differed in the duration of anti-tuberculosis treatment. Some had the minimal six-month course of triple combination therapy that included isoniazid, rifampicin and ethambutol. Others were treated with nine months of quadruple therapy (adding an initial short course of pyrazinamide). There is even a study in China which used an oral anti tuberculosis regimen of 3HRZS(E)/9HR(E) for one year combined with nasal spray combination medication of isoniazid, rifampicin and streptomycin injection solution for 3 months. However, to the best of our knowledge, there have been no published recommendations on the proper diagnosis, treatment and monitoring of response to treatment specifically for nasopharyngeal tuberculosis. While this may reflect the global rarity of the disease, further studies must be performed in tuberculosis endemic countries like the Philippines to evaluate the means of diagnosis and treatment response of nasopharyngeal tuberculosis so that management can be optimised to prevent development of multiple drug resistance.

There were at least two patients in our study with a past history of previously treated pulmonary tuberculosis. Although it is not known whether the nasopharyngeal tuberculosis appeared before or after pulmonary tuberculosis treatment, this finding could mean that the nasopharyngeal tuberculosis in these patients may not have been affected by the initial treatment given or may have developed despite treatment. Although there have been no studies that state the clear association between disseminated tuberculosis and development of multi-drug resistant tuberculosis, having multiple sites in a patient might trigger the development of resistance especially if the other sites are not known or undiagnosed. For example, a known pulmonary tuberculosis patient with a hidden or undiagnosed nasopharyngeal component will only be given six months of initial pulmonary tuberculosis treatment. Because an extrapulmonary site is involved, nasopharyngeal tuberculosis might need a longer anti-
tuberculosis treatment regimen or additional medications on top of the usual medications for pulmonary tuberculosis. The treatment for such a hypotethical patient may only be enough for the pulmonary involvement but insufficient for the nasopharyngeal disease which may lead to development of drug resistance. Moreover, should nasal endoscopy be recommended to search for nasopharyngeal masses in patients with pulmonary tuberculosis prior to treatment? Further studies are needed in this regard.

There are several limitations of our study. The purely observational and descriptive study design makes it only a preliminary study to generate epidemiological knowledge and local information among Filipinos. The study only involved a database review and it is possible that not all data were available. The study only sought to establish a local picture of nasopharyngeal tuberculosis using the limited data gathered within a tertiary general hospital. Even if it is the National University Hospital, many other regions of the country were not represented by the study population and our findings may not be generalizable to them.

In conclusion, this study suggests a relatively high prevalence rate of nasopharyngeal tuberculosis (11.6%) in patients who have a nasopharyngeal mass. Although nasopharyngeal carcinoma (62.1%) remains to be the most common diagnosis, nasopharyngeal tuberculosis should always be a differential aside from lymphoma (62.1%) remains to be the most common diagnosis, nasopharyngeal tuberculosis should always be a differential aside from lymphoma (1.8%) when confronted with a mass in the nasopharynx in areas with high tuberculosis endemicity.

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**REFERENCES**